IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	Hogan		
Serial No.:	09/613,887	Group No.:	1634
Filed:	07/11/2000	Examiner:	J. A. Goldberg
Entitled:	**METHODS AND COMPOSITIONS FOR PERIOPERATIVE GENOMIC PROFILING**		

APPELLANT'S REPLY BRIEF

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Dated: **March 1, 2010** By: /Thomas P. Vita, Jr./
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This Reply Brief is in reply to the Examiner's Answer mailed December 29, 2009 to the Appellant's Brief filed August 27, 2009.

The Commissioner is hereby authorized to charge any fees during the entire pendency of this application, including fees due under 37 C.F.R. §§ 1.16 and 1.17 that may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-4302, referencing Attorney Docket No. HOGAN-04448.

I. STATUS OF CLAIMS

Claims 106-125 and 127-191 have been rejected and are currently under appeal.

Claims 1-20 were filed in the original application. During prosecution of the application, claims 1-20 were cancelled and claims 21-41 were added in the Amendment and Response to Office Action filed August 9, 2001. Claims 21-41 were cancelled and claims 42-73 were added in the Amendment and Response to Final Office Action filed January 14, 2003. Claims 42-73 were cancelled and claims 74-105 were added in the Amendment and Response to Office Action filed January 5, 2004. Claims 74-105 were rejected in the Final Office Action dated January 11, 2005.

In an Appeal Brief filed September 19, 2005 the Appellant appealed the Final Office Action of January 11, 2005. In the Decision on Appeal mailed July 25, 2006 the Board of Patent Appeals and Interferences affirmed the rejection. Claims 74-105 were cancelled and claims 106-191 were added in an Amendment and Request for Continued Examination after Board Decision filed September 25, 2006. Claim 126 was cancelled in the Amendment and Response to Final Office Action of December 11, 2006. No other claims are pending. Therefore, claims 106-125 and 127-191 are pending in the application.

Appellant appeals the Final Office Action of May 21, 2008.

The Claims, as they now stand, are set forth in Appendix A.

II. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

There are four grounds of rejection to be reviewed on appeal:

Ground of Rejection 1 – Whether claims 106 – 124, 127-133, 135-150, 161-186, 189 and 191 are obvious over Miller (Anesthesia, Vol. 2, pages 1323-1333, 1981) (hereinafter "Miller") in view of Quane *et al*. (Human Molecular Genetics, Vol 3, No. 3, page 471-476, 1994) (hereinafter "Quane") or Acta Anaesthesiologica Scandinavica (Vol 39, page 139-141, 1995) (hereinafter "Acta") and La Du (Cellular and Molecular Neurobiology, Vol 11, No. 1, page 79-89, 1991) (hereinafter "La Du") or Pharmacogenetics (Chapter 4, pages 309-326, IDS #201) (hereinafter "Pharmacogenetics") and Evans *et al.* (Science, Vol 286, pages 487-491, October 1999) (hereinafter "Evans') or Poort *et al.* (Blood, Vol 88, No 10, page 3698-3703, 1996) (hereinafter "Poort'), and further in view of Hoon *et al.* (US Pat. 6,057,105, May 2, 2000) (hereinafter "Hoon") and Hacia (Nature Genetics Supplement, Vol. 21, pages 42-47, January, 1999) (hereinafter "Hacia").

Ground of Rejection 2 – Whether claims 151-160, 187-188, and 190 are obvious over Miller (Anesthesia, Vol. 2, pages 1323-1333, 1981) (hereinafter "Miller") in view of Quane *et al*. (Human Molecular Genetics, Vol 3, No. 3, page 471-476, 1994) (hereinafter "Quane") or Acta Anaesthesiologica Scandinavica (Vol 39, page 139-141, 1995) (hereinafter "Acta") and La Du (Cellular and Molecular Neurobiology, Vol 11, No. 1, page 79-89, 1991) (hereinafter "La Du") or Pharmacogenetics (Chapter 4, pages 309-326, IDS #201) (hereinafter "Pharmacogenetics") and Evans *et al.* (Science, Vol 286, pages 487-491, October 1999) (hereinafter "Evans') or Poort *et al.* (Blood, Vol 88, No 10, page 3698-3703, 1996) (hereinafter "Poort'), and further in view of Hoon *et al.* (US Pat. 6,057,105, May 2, 2000) (hereinafter "Hoon") and Hacia (Nature Genetics Supplement, Vol. 21, pages 42-47, January, 1999) (hereinafter "Hacia") as applied to claims 106 – 124, 127-133, 135-150, 161-186, 189 and 191 above, and further in view of Lapointe *et al*. (US 6,678,669, January, 2004) (hereinafter "LaPointe").

Ground of Rejection 3 – Whether Claim 185 is obvious over Miller (Anesthesia, Vol. 2, pages 1323-1333, 1981) (hereinafter "Miller") in view of Quane *et al.* (Human Molecular Genetics, Vol 3, No. 3, page 471-476, 1994) (hereinafter "Quane") or Acta Anaesthesiologica Scandinavica (Vol 39, page 139-141, 1995) (hereinafter "Acta") and La Du (Cellular and Molecular Neurobiology, Vol 11, No. 1, page 79-89, 1991) (hereinafter "La Du") or Pharmacogenetics (Chapter 4, pages 309-326, IDS #201) (hereinafter "Pharmacogenetics") and Evans *et al.* (Science, Vol 286, pages 487-491, October 1999) (hereinafter "Evans') or Poort *et al.* (Blood, Vol 88, No 10, page 3698-3703, 1996) (hereinafter "Poort'), and further in view of Hoon *et al.* (US Pat. 6,057,105, May 2, 2000) (hereinafter "Hoon") and Hacia (Nature Genetics Supplement, Vol. 21, pages 42-47, January, 1999) (hereinafter "Hacia") as applied to claims 106 – 124, 127-133, 135-150, 161-186, 189 and 191 above, and further in view of Lyamichev *et al.* (Nature Biotechnology, Vol. 17, pages 292-296, March, 1999) (hereinafter "Lyamichev").

Ground of Rejection 4 – Whether claims 125 and 134 are obvious over Miller (Anesthesia, Vol. 2, pages 1323-1333, 1981) (hereinafter "Miller") in view of Quane *et al.* (Human Molecular Genetics, Vol 3, No. 3, page 471-476, 1994) (hereinafter "Quane") or Acta Anaesthesiologica Scandinavica (Vol 39, page 139-141, 1995) (hereinafter "Acta") and La Du (Cellular and Molecular Neurobiology, Vol 11, No. 1, page 79-89, 1991) (hereinafter "La Du") or Pharmacogenetics (Chapter 4, pages 309-326, IDS #201) (hereinafter "Pharmacogenetics") and Evans *et al.* (Science, Vol 286, pages 487-491, October 1999) (hereinafter "Evans') or Poort *et al.* (Blood, Vol 88, No 10, page 3698-3703, 1996) (hereinafter "Poort'), and further in view of Hoon *et al.* (US Pat. 6,057,105, May 2, 2000) (hereinafter "Hoon") and Hacia (Nature Genetics Supplement, Vol. 21, pages 42-47, January, 1999) (hereinafter "Hacia") as applied to claims 106 – 124, 127-133, 135-150, 161-186, 189 and 191 above, and further in view of the specification (Tables 1-4).

III. ARGUMENT

A. Claims 106 – 124, 127-133, 135-150, 161-186, 189 and 191 are not obvious over Miller in view of Quane or Acta and La Du, or Pharmacogenetics and Evans, or Poort, and further in view of Hoon and Hacia.

The present invention claims perioperative genomic profiles comprising assays in two or more nucleic acid makers in two or more genes associated with two or more conditions of use in determining the risk for complications during a surgical procedure. The Office asserts that the claims are obvious over the Office's combination of nine references. The Appellant asserts that they are not for not just one but multiple reasons.

The Appellant asserts that the Office has erred in resolving the level of ordinary skill in the pertinent art. This problem is not resolved in the Examiner's answer. For example, the Examiner notes "An ordinary artisan would encompass a molecular biologist who performs diagnostic assays as well as an anesthesiologist." (Examiner's Answer, page 23). The Appellant notes that no such ordinary artisan exists. Clearly anesthesiologists of ordinary skill, and molecular biologists who perform diagnostic assays of ordinary skill, differ in education and experience. Moreover, the types of problems encountered by molecular diagnosticians and anesthesiologists are broadly different, as are the types of solutions to these problems. The Examiner has expressly recognized anesthesiologists and other perioperative clinicians as artisans of ordinary skill during prosecution of the present application. Accordingly the Appellant has provided factual evidence that the ordinary artisan did not recognize the benefit of testing an individual prior to surgery and subjection to anesthesia for known genetic markers associated with conditions triggered by anesthesia or surgery at the time the invention was made (Second Declaration of Kirk Hogan M.D, page 2), and that those of ordinary skill in the art *i.e.*, anesthesiologists and surgeons, did not arrive at the solution of the presently claimed invention. (Declaration of Dr. Coursin of June 10, 2007, page 2.) The Office has never provided evidence contradicting these evidential statements of fact. In turn, the Office has not provided evidence that the molecular diagnostician of ordinary skill is also a skilled artisan in perioperative care. The Appellant submits that in equating "an ordinary artisan in the biochemical fields" (Examiner's Answer, page 15) with, for example, a skilled doctor "subject to liability"

(Examiner's Answer, page 31), the author has created hybrid that fails to fulfill the Office's duty under *Graham v. John Deere Co*.

The Appellant further asserts that in the Examiner's Answer the Office has erred in determining the scope and contents of the prior art, and in ascertaining differences between the prior art and claims at issue. For example, the Examiner has never identified the elements "selecting a perioperative course of action" (claim 106), a "first surgical procedure for said subject" (claim 107), "a presymptomatic diagnosis" (claim 120), "selecting a surgical treatment course of action" (claim 127), "said surgical procedure is non-invasive surgery" (claims 139 and 179), "selection of monitoring procedures" (claim 148 and 175), "distributing said results of said patient's genomic profile according to said patient's preference" (claims 149 and 189), and "distributing said patient's sample according to said patient's preference (claims 149 and 189) in the prior art, either alone or in combination. To the contrary, the Examiner addresses each of the missing elements under an improperly applied "common sense" standard ("The examiner instead relies upon common sense.", Examiner's Answer, page 35), quoting "KSR finds that "rigid preventative rules that deny recourse to common sense are neither necessary under, nor consistent with, this Court's case law." (Examiner's answer, page 33.) While common sense as a source of reasons to combine or modify prior art references is considered in KSR, KSR does not permit the Office to employ "common sense" as a source for missing elements lacking in the prior art references themselves without evidence, specificity and findings of fact.

The Appellant observes that in proffering this standard, the Examiner has misread KSR and created a novel, personal, and unsupported test for obviousness. As pointed out to the Examiner at multiple points in the Appellant's Brief (see, for example, page 39), the Office may not respond to the fact of missing elements in the Office's combination of references with an argument based on the Office's speculations of what an ordinary artisan would or would not have been motivated to do in the absence of evidence of record. The Examiner's Answer in reply is silent in every instance. The Appellant asserts that nothing in KSR or other case law, statute, MPEP or other authority grants the Office permission to assign missing claim elements to the Office's notion of "common sense" based, for example, on the presence or absence of professional malpractice ("Doctors are subject to liability", Examiner's Answer, page 31). Failure of the Examiner's combination to teach or suggest each and every element of a claim precludes an obviousness rejection under 35 U.S.C. § 103. Section 2143.03 of the MPEP

requires the consideration of every claim feature in an obviousness determination. To render a claim unpatentable, the Office's combination of cited art must teach or suggest each and every feature of the claims. (*In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). The Board of Patent Appeal and Interferences has recently confirmed that a proper obviousness determination requires that an Examiner make "a searching comparison of the claimed invention – including all its limitations – with the teaching of the prior art." (*In re Wada and Murphy*, Appeal 2007-3733, *citing In re Ochiai*, 71 F.3d 1565, 1572 (Fed. Cir. 1995) (Emphasis in original.). The Supreme Court has long held that obviousness is a question of law based on underlying factual inquiries, including … ascertaining the differences between the claimed invention and the prior art. (*Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966) In turn, MPEP 904 instructs Examiners to conduct an art search that covers "the invention as described and claimed." Accordingly, a finding of obviousness requires at least a suggestion of all of the features in a claim. (*In re Wada and Murphy*, *citing CFMT, Inc. v. Yieldup Intern. Corp.*, 349 F.3d 1333, 1342 (Fed. Cir. 2003), and *In re Royka*, 490 F.2d 981, 985 (CCPA 1974)).

The Appellant notes that in addition to the missing elements found only in the Examiner's "common sense", the Examiner's Answer fails to identify numerous other missing elements. For example, in response to the Appellant's notice of the missing element "unique genomic identifier" in claim 191, the Examiner argues "The combination of references undeniably comprises selecting markers of pharmacogenetic risk, genetic markers of outcomes of a surgical procedure, genetic markers to predict postoperative outcomes, as also recited in Claim 191. Thus, there is no missing element." (Examiner's Answer, page 42.) The Specification defines unique genomic identifiers as: "a unique genomic identifier (e.g., a series of polymorphic non-coding SNPs), thus providing a secure, accurate internal reference for archiving and tracking genetic data specific to the particular subject." (Specification lines 9-12, page 30). The Appellant notes that this element is missing from the Examiner's combination of references, as are administration of anesthesia during a medical procedure (claims 117 and 168), differential diagnosis of co-existing diseases (claim 121), obtaining consent to obtain and assay a perioperative subject for genetic variations (claim 149), computer programs comprising instructions which direct a processor to analyze the results of the genomic profile (claim 150 and claims dependent thereupon), variant alleles of MTR, MTRR, and CBS (claims 173 and 174), kits with a computer program on a computer readable medium comprising instructions which

direct a processor to analyze data derived from use of said reagents (*i.e.*, not the "computer program" of the Examiner Answer, page 40) (claim 186), kits which generate a genomic profile using the claimed grouping of genes (claim 186), and selecting markers for inclusion on a perioperative genomic profile based on analytical validity, clinical validity and clinical utility (claim 189).

The Appellant asserts that the Examiners' Answer fails to meet the Patent and Tradermark Office's burden to provide a suggestion or motivation to one of skill in the art to combine the elements to yield the claimed invention at the time the invention was made. The Examiner concedes that Quane is directed to a single gene (*RYR1*) and a single condition (malignant hyperthermia), but persists in using Quane as motivation to combine the Examiner's references to arrive at the perioperative genomic profiles of the presently claimed in invention. (Examiner's Answer pages 4, and 20-21.) Nor has the Examiner explained the relevance of Quane to claims 160 and 182 which do not recite *RYR1*. Clearly, as evidenced by the Declarations of Dr. Hogan and Dr. Coursin) neither Quane, nor any other of the Examiner's references, or any other source taught or suggested the perioperative genomic profiles of the present invention. Contrary, to the Examiner's arguments, the motivation to combine the Examiners' references comes only from the Appellant's disclosure in possession of the Examiner.

B. Claims 151-160, 187-188 and 190 are not obvious over Miller in view of Quane or Acta and La Du, or Pharmacogenetics and Evans, or Poort, and further in view of Hoon and Hacia, and further in view of LaPointe.

The Appellant asserts that the Office has erred in resolving the level of ordinary skill in the pertinent art. For example, the Examiner notes "An ordinary artisan would encompass a molecular biologist who performs diagnostic assays as well as an anesthesiologist." (Examiner's Answer, page 23). The Appellant notes that an improper "ordinary artisan" analysis has been applied as discussed above. The problem is exacerbated with the present rejection as the Examiner requires that the ordinary artisan has computer skills able to design "a neural network as taught by LaPointe." (Examiner's Answer, page 14.) The Office has not properly identified the ordinary artisan, nor viewed the prior art from the proper perspective.

Nor does the addition of Lapointe remedy missing elements in the Examiner's combination of references. For example, neither LaPointe nor any other of the Examiner's references alone or in combination teach or suggest computer instructions that translate results into information of predictive value for a clinician (claim 151), computer instructions that translate results into a risk assessment for treatment options (claim 152), computer instructions that translate results into recommendations for treatment options (claim 153), computer instructions that generate a report for display to a clinician (claim 154), a display in the form of a report that can be printed (claim 155), a display in the form of a report on a computer monitor (claim 156), computer instructions that are sufficient to receive, process and transmit results of the perioperative genomic profile to and from said patient, a clinical laboratory and medical personnel (claim 157), transmission of the results using an electronic communication system (claim 158), an electronic communication system that transmits said results to a distant computer system for processing (claim 159), computer instructions that comprise information to optimize perioperative care that, based on at least the presence of variant alleles of two or more genes associated with two or more conditions selected from the group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS,* and *TNFα,* directs said clinician to a specific perioperative clinical pathway for said patient (claim 160), encrypting the results of a perioperative genomic profile with privacy security protocols (claim 187), or decoding the results of a perioperative genomic profile with privacy security protocols (claim 188). As well, the Examiner notes "With respect of Claim 190, Appellant asserts that the art does not teach distributing the results of a patient profile according to the patient's preference. Upon review of Claim 190, the claim does not require any patient preferences." (Examiner's Answer, page 44). The Examine is in error. Claim 190 depends upon claim 189 which recites patient's preferences.

C. Claim 185 is not obvious over Miller in view of Quane or Acta and La Du, or Pharmacogenetics and Evans, or Poort, and further in view of Hoon and Hacia, and further in view of Lyamichev.

The Appellant asserts that the Office has erred in resolving the level of ordinary skill in the pertinent art for the reasons noted above.

D. Claim 125 and 134 are not obvious over Miller in view of Quane or Acta and La Du, or Pharmacogenetics and Evans, or Poort, and further in view of Hoon and Hacia, and further in view of the Specification.

As noted in the Appellant's Brief, the Examiner's combination of references fails to disclose not just one, but multiple elements of the claimed invention. For example, the Office's combination of references fails to teach or suggest the closed panel of alleles in genes encoding BChE, CYP2D6, MTHFR, MTR, CBS, F2, F5, RYR1, CACNA1S, and CPT2, and TNFα of claims 125 and 134. The references cited by the office provide alleles in one, or at most, two genes encoding the claimed proteins, but not this specific combination of 11 proteins and no other. Nor has the Office provided evidence or reasoning why this specific combination as a claim element is obvious in view of "any number of genes" to which the Final Office Action of May 21, 2008 refers. The Appellant asserts that there is nothing in the Office's combination of references or elsewhere in the prior art that teaches or suggests this combination of alleles as a limitation. The Appellant further asserts that this selected combination is clearly not known in the art, and that the Examiner has failed to provide support for the obviousness of the combination.

As well, none of the Office's cited alleged prior art references, alone or in combination, teach or suggest reagents sufficient to detect the presence or absence of variant alleles in the gene encoding methionine synthase (*MTR*). None of the Office's cited alleged prior art references, alone or in combination, teach or suggest reagents sufficient to detect the presence or absence of variant alleles in the gene encoding methionine synthase reductase (*MTRR*). None of the Office's alleged prior art references, alone or in combination, teach or suggest reagents sufficient to detect the presence or absence of variant alleles in the gene encoding cystathionine beta-synthase (*CBS*). None of the Office's alleged prior art references, alone or in combination, teach or suggest reagents sufficient to detect the presence or absence of variant alleles in the gene encoding carnitine palmitoyl transferase II (*CPT2*). In response, the Examiner's reply is silent.

IV. CONCLUSION

For the foregoing reasons, Appellant respectfully submits that the Office's rejections of claims 106-125 and 127-191 are erroneous. Reversal of the rejections is respectfully requested. Appellant requests that the Board render a decision as to the allowability of the Claims.

Respectfully submitted,

Dated: March 1, 2010

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APPENDIX A

PENDING CLAIMS

1. – 105. (cancelled)

106. (previously presented) A method of screening a patient perioperatively to determine a risk for complications during a surgical procedure associated with known genetic variations comprising:

a) obtaining a sample from a perioperative subject, said perioperative subject being a patient scheduled for a surgical procedure that has not yet completed said surgical procedure; and

b) subjecting said sample to an assay for detecting two or more nucleic acid genetic markers in two or more genes associated with two or more conditions to generate a genomic profile;

c) selecting a perioperative course of action based on information from said genomic profile, wherein said subjecting step occurs after said patient is scheduled for surgery but before completion of said surgical procedure, thereby determining a risk for complications during said surgical procedure; and

d) performing said surgical procedure wherein said perioperative course of action is used by at least one of the group consisting of an anesthesiologist, a nurse, and a surgeon.

107. (previously presented) The method of Claim 106, wherein said surgical procedure is the first surgical procedure for said subject.

108. (previously presented) The method of Claim 106, wherein previous said surgical procedures on said patient have been with one or more complications.

109. (previously presented) The method of Claim 106, wherein said course of action comprises administration of anesthesia during a surgical procedure.

110. (previously presented) The method of Claim 109, wherein said anesthesia is general anesthesia.

111. (previously presented) The method of Claim 110, wherein said general anesthesia is inhalational anesthesia.

112. (previously presented) The method of Claim 110, wherein said general anesthesia is intravenous anesthesia.

113. (previously presented) The method of Claim 109, wherein said anesthesia is regional anesthesia.

114. (previously presented) The method of Claim 113, wherein said regional anesthesia is spinal or epidural anesthesia.

115. (previously presented) The method of Claim 106, wherein said surgical procedure is non-invasive surgery.

116. (previously presented) The method of Claim 106, wherein said surgical procedure is invasive surgery.

117. (previously presented) The method of Claim 106, wherein said course of action comprises administration of anesthesia during a medical procedure.

118. (previously presented) The method of Claim 106, wherein said genomic profile comprises information pertaining to a pharmacodynamic risk.

119. (previously presented) The method of Claim 106, wherein said genomic profile comprises information pertaining to a pharmacokinetic risk.

120. (previously presented) The method of Claim 106, wherein said genomic profile comprises a presymptomatic diagnosis.

121. (previously presented) The method of Claim 106, wherein said genomic profile comprises information pertaining to differential diagnosis of co-existing diseases.

122. (previously presented) The method of Claim 106, wherein said two or more nucleic acid genetic markers comprise mutations in two or more genes, said genes selected from the group consisting of *BChE*, *CYP2D6*, *MTHFR*, *MTR*, *CBS*, *F2, F5*, *RYR1*, *CACNA1S*, and *CPT2*.

123. (previously presented) The method of Claim 122, wherein said two or more nucleic acid genetic markers comprise 5 or more mutations in two or more genes.

124. (previously presented) The method of Claim 122, wherein said two or more nucleic acid genetic markers comprise 10 or more mutations in two or more genes.

125. (previously presented) The method of Claim 106, wherein said genomic profile consists of alleles in genes encoding BChE, CYP2D6, MTHFR, MTR, CBS, F2, F5, RYR1, CACNA1S, and CPT2, and TNFα.

126. (cancelled)

127. (previously presented) A method for selecting conditions for a surgical procedure by screening a patient perioperatively to determine a risk for complications during a surgical procedure associated with known genetic variations comprising:

a) providing a sample from a perioperative subject, said perioperative

subject being a patient scheduled for a surgical procedure that has not yet completed said surgical procedure;

b) subjecting said sample to an assay for detecting two or more nucleic acid genetic markers in two or more genes known to be associated with two or more perioperative phenotypes to generate a genomic profile;

c) selecting a surgical procedure treatment course of action based on information from said genomic profile; and

d) subjecting said subject to a surgical procedure.

128. (previously presented) The method of Claim 127, wherein said genetic markers are associated with a pharmacological response.

129. (previously presented) The method of Claim 128, wherein said pharmacological response is to an anesthetic.

130. (previously presented) The method of Claim 128, wherein said pharmacological response is to drugs used in anesthetic practice.

131. (previously presented) The method of Claim 127, wherein said two or more nucleic acid genetic markers comprises a mutation in two or more genes associated with two or more conditions, said genes selected from the group consisting of *BChE, CYP2D6, MTHFR, MS, CBS, F2, F5, RYR1, CACNA1S, and CPT 2.*

132. (previously presented) The method of claim 131, wherein said two or more nucleic acid genetic markers comprises 5 or more mutations in two or more genes.

133. (previously presented) The method of claim 131, wherein said two or more nucleic acid genetic markers comprises 10 or more mutations in two or more genes.

134. (previously presented) The method of Claim 127, wherein said genomic profile consists of alleles in genes encoding BChE, CYP2D6, MTHFR, MTR, CBS, F2, F5, RYR1, CACNA1S, and CPT2, and TNFα.

135. (previously presented) A method of screening a patient perioperatively to determine a risk for complications during a surgical procedure from known genetic variations comprising:

a) obtaining a sample from a perioperative subject, said perioperative subject being a patient scheduled for a surgical procedure that has not yet completed said surgical procedure; and

b) subjecting said sample to an assay for detecting genetic markers in genes clinically associated with conditions consisting of butyrylcholinesterase deficiency, impaired debrisoquine metabolism, sepsis, thrombosis, and malignant hyperthermia to generate a genomic profile;

c) directing a physician to a perioperative treatment course of action based on information from said genomic profile for determining a risk for complications during a surgical procedure; and

d) subjecting said subject to a surgical procedure.

136. (previously presented) The method of Claim 135, wherein said physician is an anesthesiologist.

137. (previously presented) The method of Claim 135, wherein said course of action comprises administration of anesthesia during a surgical procedure.

138. (previously presented) The method of Claim 135, wherein said physician is a surgeon.

139. (previously presented) The method of Claim 135, wherein said surgical procedure is non-invasive surgery.

140. (previously presented) The method of Claim 135, wherein said surgical procedure is invasive surgery.

141. (previously presented) The method of Claim 135, wherein the said two or more nucleic acid genetic markers comprises 5 or more mutations in two or more genes.

142. (previously presented) The method of Claim 135, wherein the said two or more nucleic acid genetic markers comprises 10 or more mutations in two or more genes.

143. (previously presented) A method of screening a patient perioperatively to determine a risk for complications during a surgical procedure from known genetic variations comprising:

a) obtaining a sample from a perioperative subject, said perioperative subject being a patient scheduled for a surgical procedure that has not yet completed said surgical procedure;

b) subjecting said sample to an assay for detecting two or more nucleic acid genetic markers in two or more genes clinically associated with butyrylcholinesterase deficiency and impaired debrisoquine metabolism to generate a genomic profile:

c) directing a physician to a perioperative treatment course of action based on information from said genomic profile for determining a risk for complications during a surgical procedure; and

d) subjecting said subject to a surgical procedure.

144. (previously presented) A method for selecting an appropriate anesthesia treatment during surgery, comprising:

a) providing a sample from a perioperative subject, said perioperative subject being a patient scheduled for a surgical procedure that has not yet completed said surgical procedure;

b) subjecting said sample to an assay that detects a first marker in a

first gene and a second marker in a second gene to generate assay results, wherein said markers are known to be associated with adverse responses to anesthesia treatment; and

c) subjecting said subject to a surgical procedure, wherein said assay results are consulted by a physician in selecting an appropriate anesthesia treatment for said subject based on information from said assay results.

145. (previously presented) The method of Claim 144, wherein said physician is an anesthesiologist.

146. (previously presented) The method of Claim 144, wherein said selecting comprises selection of dosages of anesthesia.

147. (previously presented) The method of Claim 144, wherein said selecting comprises selection of anesthesia compounds.

148. (previously presented) The method of Claim 144, wherein said selecting comprises selection of monitoring procedures.

149. (previously presented) A method for providing a perioperative course of action to a clinician based on a patient's risk for complications during and after a surgical procedure associated with known genetic variations, comprising:

a) obtaining consent from a patient to obtain and assay a sample from a perioperative subject for genetic variations, said patient being a patient scheduled for a surgical procedure that has not yet completed said surgical procedure;

b) obtaining said sample from said patient;

c) forwarding said sample to a clinical laboratory;

d) isolating DNA from said sample in said clinical laboratory;

e) subjecting said DNA to an assay in said clinical laboratory for detecting two or more nucleic acid genetic markers in two or more genes associated with

two or more conditions to generate a genomic profile wherein said subjecting step occurs after said patient is scheduled for surgery but before completion of said surgical procedure;

f) forwarding the results of said genomic profile to said clinician;

g) directing said clinician to a perioperative course of action for said patient based on said risk for complications during and after said surgical procedure based on information from said genomic profile;

h) subjecting said patient to a surgical procedure based on said perioperative course action;

i) distributing said results of said patient's said genomic profile according to said patient's preference wherein said distributing is selected from the group consisting of destroying said results, saving said results for future access by said patient, saving said results for future access by said clinician, and donating said results for research; and

j) distributing said patient's said sample according to said patient's preference wherein said distributing is selected from the group consisting of destroying said sample, saving said sample for future access, and donating said sample for research.

150. (previously presented) The method of Claim 149, wherein said directing said clinician to said perioperative course of action comprises a computer program comprising instructions which direct a processor to analyze said results of said genomic profile.

151. (previously presented) The method of Claim 150, wherein said instructions translate said results into information of predictive value for a clinician.

152. (previously presented) The method of Claim 150, wherein said instructions translate said results into a risk assessment for treatment options.

153. (previously presented) The method of Claim 150, wherein said instructions translate said result into recommendations for treatment options.

154. (previously presented) The method of Claim 150, wherein said instructions generate a report for display to a clinician.

155. (previously presented) The method of Claim 154, wherein said display is in the form of a report that can be printed.

156. (previously presented) The method of Claim 154, wherein said display is in the form of a report on a computer monitor.

157. (previously presented) The method of Claim 150, wherein said instructions are sufficient to receive, process and transmit said results of said genomic profile to and from said patient, a clinical laboratory and medical personnel.

158. (previously presented) The method of Claim 157, wherein said transmission of said results uses an electronic communication system.

159. (previously presented) The method of Claim 158, wherein said electronic communication system transmits said results to a distant computer system for processing.

160. (previously presented) The method of Claim 150, wherein said instructions comprise information to optimize perioperative care that, based on at least the presence of variant alleles of two or more genes associated with two or more conditions selected from the group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS,* and *TNFα,* directs said clinician to a specific perioperative clinical pathway for said patient.

161. (previously presented) The method of Claim 149, wherein said perioperative course of action is an anesthesia treatment course of action.

162. (previously presented) The method of Claim 161, wherein said anesthesia treatment course of action is a general anesthesia course of action.

163. (previously presented) The method of Claim 162, wherein said general anesthesia treatment course of action is an inhalational anesthesia treatment course of action.

164. (previously presented) The method of Claim 162, wherein said general anesthesia treatment course of action is an intravenous anesthesia treatment course of action.

165. (previously presented) The method of Claim 162, wherein said general anesthesia treatment course of action is a combined inhalational and intravenous anesthesia treatment course of action.

166. (previously presented) The method of Claim 161, wherein said anesthesia treatment course of action is a regional anesthesia treatment course of action.

167. (previously presented) The method of Claim 161, wherein said anesthesia treatment course of action is a combined regional and general anesthesia treatment course of action.

168. (previously presented) The method of Claim 149, wherein said perioperative treatment course of action is an anesthesia course of action during a medical procedure.

169. (previously presented) The method of Claim 149, wherein said perioperative treatment course of action comprises selection of dosages of analgesic compounds.

170. (previously presented) The method of Claim 169, wherein said selection comprises increasing the dosage of analgesic compounds metabolized by CYP2D6.

171. (previously presented) The method of Claim 169, wherein said selection comprises decreasing the dosage of analgesic compounds metabolized by CYP2D6.

172. (previously presented) The method of Claim 149, wherein said perioperative treatment course of action comprises prophylaxis for thrombosis.

173. (previously presented) The method of Claim 172, wherein said prophylaxis comprises increasing prophylaxis for thrombosis associated with variant alleles of *F5, F2, MTHFR, MTR, MTRR,* and *CBS.*

174. (previously presented) The method of Claim 172, wherein said prophylaxis comprises decreasing prophylaxis for thrombosis associated with variant alleles of *F5, F2, MTHFR, MTR, MTRR,* and *CBS.*

175. (previously presented) The method of Claim 149, wherein said perioperative course of action comprises monitoring procedures.

176. (previously presented) The method of Claim 149, wherein said perioperative course of action comprises pre-operative phenotypic tests and consultations.

177. (previously presented) The method of Claim 149, wherein said risk of complications provides a prognosis after an anesthesia treatment course of action.

178. (previously presented)The method of Claim 149, wherein said perioperative course of action is a surgical treatment course of action.

179. (previously presented) The method of Claim 178, wherein said surgical treatment course of action is a non-invasive surgical treatment course of action.

180. (previously presented) The method of Claim 178, wherein said surgical treatment course of action is an invasive surgical treatment course of action.

181. (previously presented) The method of Claim 149, wherein said risk of complications provides a prognosis after a surgical treatment course of action.

182. (previously presented) The method of Claim 149, wherein said perioperative treatment course of action comprises a post-operative treatment course of action.

183. (previously presented) The method of Claim 149, wherein said perioperative treatment course of action directs a clinician to a specific clinical pathway of medical intervention for said patient.

184. (previously presented) The method of Claim 149, wherein said perioperative treatment course of action directs a clinician to a specific clinical pathway of anesthesia intervention for said patient.

185. (previously presented)The method of Claim149, wherein said assay comprises structure-specific cleavage of oligonucleotide probes assay.

186. (previously presented) The method of Claim 149, wherein said subjecting said DNA to an assay further comprises:

i. providing a kit for generating a perioperative genomic profile for a subject, comprising:

a) reagents configured such that when exposed to a sample containing target nucleic acid from a perioperative subject, said subject being a patient scheduled for a surgical procedure that has not yet completed said surgical procedure, are sufficient to detect the presence or absence of variant alleles in two or more genes associated with two or more conditions selected from the group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS,* and *TNF*α so as to generate a genomic profile for use in selecting a perioperative course of action for said subject; and

b) a computer program on a computer readable medium

comprising instructions which direct a processor to analyze data derived from use of said reagents; and

ii. generating said genomic profile with said kit.

187. (previously presented) The method of Claim 149, further comprising the step of encrypting said results of said genomic profile with privacy security protocols.

188. (previously presented) The method of Claim 149, further comprising the step of decoding said results of said genomic profile with privacy security protocols.

189. (previously presented) A method of screening a patient perioperatively to determine a risk for complications during a surgical procedure associated with known genetic variations comprising:

a) obtaining a sample from a perioperative subject, said perioperative subject being a patient scheduled for a surgical procedure that has not yet completed said surgical procedure;

b) subjecting said sample to an assay for detecting two or more nucleic acid genetic markers in two or more genes associated with two or more conditions to generate a genomic profile, wherein said markers are selected by the criteria of analytical validity, clinical validity and clinical utility;

c) selecting a perioperative course of action based on information from said genomic profile, wherein said subjecting step occurs after said patient is scheduled for surgery but before completion of said surgical procedure, thereby determining a risk for complications during said surgical procedure;

e) distributing said results of said patient's said genomic profile according to said patient's preference wherein said distributing is selected from the group consisting of destroying said results, saving said results for future access by said paitent, saving said results for future access by said clinician, and donating said results for research; and

f) distributing said patient's said sample according to said patient's preference wherein said distributing is selected from the group consisting of

destroying said sample, saving said sample for future access, and donating said sample for research.

190. (previously presented) The method of Claim 189, wherein said selecting of markers, said subjecting said sample to said assay, and said distributing of said results of said patient's said genomic profile is organized by an integrated electronic system.

191. (previously presented) The method of Claim 189, further comprising the step of selecting said genetic markers from the group consisting of genetic markers of pharmacogenetic risk, genetic markers of co-existing symptomatic conditions, genetic markers of co-existing non-symptomatic conditions, genetic markers of outcomes of a surgical procedure, genetic markers of a patient in a specific group, genetic markers that predict postoperative outcomes, and genetic markers consisting of unique genomic identifiers.